

Exhibit D

February 28, 2019

Robert W. Carlson, MD
National Comprehensive Cancer Network

Clifford A. Hudis, MD
American Society of Clinical Oncology

Martha Liggett, Esq.
American Society of Hematology

Dear Dr. Carlson, Dr. Hudis, and Ms. Liggett,

Thank you for your letter regarding CDC's *Guideline for Prescribing Opioids for Chronic Pain*. CDC greatly appreciates your feedback regarding the interpretation of the Guideline, particularly with regard to patients undergoing cancer treatment, cancer survivors who have chronic pain, and individuals with sickle cell disease.

The Guideline was developed to provide recommendations for primary care clinicians who prescribe opioids for chronic pain outside of active cancer treatment, palliative care, and end-of-life care. Because of the unique therapeutic goals, and balance of risks and benefits with opioid therapy in such care, clinical practice guidelines specific to cancer treatment, palliative care, and end of life care should be used to guide treatment and reimbursement decisions regarding use of opioids as part of pain control in these circumstances.

The Guideline may apply to cancer survivors in specific conditions, namely, when these patients experience chronic pain after completion of cancer treatment, are in clinical remission, and are under cancer surveillance only. As you note, for select groups of cancer survivors with persistent pain due to past cancer or past cancer treatment, the relationship of benefits to risks in use of opioids for chronic pain is unique. Clinical practice guidelines addressing pain control for cancer survivors, such as the 2016 *American Society of Clinical Oncology Clinical Practice Guideline on Management of Chronic Pain in Survivors of Adult Cancers* and the 2018 *National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology: Adult Cancer Pain*, have been published subsequent to release of CDC's *Guideline for Prescribing Opioids for Chronic Pain*. Such guidelines provide useful guidance on unique considerations for use of opioids for pain control in cancer survivors.

As you additionally note, unique considerations in sickle cell disease can change the balance of benefits and risks for the use of opioids in pain management. Given the challenges of managing the painful complications of sickle cell disease, clinical practice guidelines addressing use of opioids as part of pain control in patients with sickle cell disease should be used to guide treatment and reimbursement decisions. The CDC Guideline refers readers to NIH's *National Heart, Lung, and Blood Institute's Evidence Based Management of Sickle Cell Disease Expert Panel Report for guidance for management of sickle cell disease*. This resource can be found at <https://www.nhlbi.nih.gov/health-topics/evidence-based-management-sickle-cell-disease>.



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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The Guideline is not intended to deny any patients who suffer with chronic pain from opioid therapy as an option for pain management. Rather, the Guideline is intended to ensure that clinicians and patients consider all safe and effective treatment options for patients. Clinical decision-making should be based on the relationship between the clinician and patient, with an understanding of the patient's clinical situation, functioning, and life context, as well as a careful consideration of the benefits and risk of all treatment options, including opioid therapy. CDC encourages physicians to continue to use their clinical judgment and base treatment on what they know about their patients, including the use of opioids if determined to be the best course of treatment. Providers should communicate frequently with their patients to discuss both the benefits and risks of opioid therapy and revisit treatment plans for pain regularly to achieve the most positive outcomes for patients.

CDC has developed translational materials and trainings for providers to continue to emphasize that the Guideline is intended for primary care physicians for the treatment of chronic pain. Some of these resources include:

- *Assessing Benefits and Harms of Opioid Therapy:*
https://www.cdc.gov/drugoverdose/pdf/Assessing_Benefits_Harms_of_Opioid_Therapy-a.pdf.
- CDC Training Series *Applying CDC's Guideline for Prescribing Opioids*, a web-based training to help providers gain a deeper understanding of the Guideline. Trainings address a variety of topics, including provider-patient communication and decision-making on initiating opioids for chronic pain. <https://www.cdc.gov/drugoverdose/training/online-training.html>

Chronic pain is common and multidimensional, and patients deserve safe and effective pain management. Collaborative relationships between patients and providers are critical to provide optimal pain management. CDC will continue to emphasize what the Guideline and associated materials say about communication, patient engagement in decision-making, and maintenance of the patient-provider relationship.

CDC will revisit the Guideline as new evidence and recommendations become available to determine when gaps have been sufficiently closed to warrant an update. We value stakeholder input to assist with such an update.

Sincerely,

Deborah Dowell, MD, MPH

Chief Medical Officer

The National Center for Injury Prevention and Control
Centers for Disease Control and Prevention